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AMENDMENT UNDER 37 C.F.R. §1.111	Attorney Docket	10981620-1
	First Named Inventor	Glenda C. DELENSTARR
	Application Number	09/398,399
	Filing Date	September 17, 1999
	Group Art Unit	1655
Address to: Assistant Commissioner for Patents Washington, D.C. 20231	Examiner Name	B. Sisson
	Title	TECHNIQUES FOR ASSESSING NONSPECIFIC BINDING OF NUCLEIC ACIDS TO SURFACES

Sir:

This amendment is responsive to the Office Action dated April 26, 2000 for which a three-month period for response was given making this response due on or before July 26, 2000. In view of the amendments to the specification and claims and the remarks put forth below, reconsideration and allowance are respectfully requested.

AMENDMENTS

IN THE SPECIFICATION

Page 30, line 30, please replace "Triton X-100" with --TRITON™ X-100 (polyoxyethylene(10) isooctylphenyl ether)--.

IN THE CLAIMS

Please cancel claims 5-9 and 33; amend claims 10-32; and add new claims 34-39 as shown below.

Cancel claims 5-9.

10. (Amended) A [method of detecting the presence and/or amount of a target nucleotide sequence in an analyte] hybridization assay, said [method] assay comprising:

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(a) providing [an analyte suspected of containing the] a sample of labeled target [nucleotide sequence] nucleic acids;

(b) contacting [an aliquot of] said [analyte] sample under stringent hybridization conditions [suspected of containing said target nucleotide sequence] with a [set] collection of substrate bound nucleic acid features comprising [oligophosphodiester probes, wherein said target nucleotide sequence is labeled with a detectable label capable of generating a measurable signal, and further wherein said features comprise]:

(i) [hybridization features comprising] hybridization probes [that selectively hybridize to said labeled target nucleotide sequence], and

ii) background features [comprising background probes that do not selectively hybridize to said labeled target nucleotide sequence];

(c) removing unhybridized target nucleic acids from said substrate;

([c]d) detecting an observed signal[, wherein the observed signal is an amount of signal generated from contacting the target nucleotide sequence with said features comprising oligophosphodiester probes] for each resultant detectable hybridization probe feature of said substrate;

([d]e) [detecting] determining a background signal[, wherein said background] by detecting a signal [is an amount of signal generated from said background features] for each background feature and averaging said background feature signals;

([e]f) subtracting the background signal from the observed signal [to determine the presence and/or amount of said target nucleotide sequence in said analyte] for each hybridization probe feature.

11. (Amended) The [method] assay of claim 10 wherein said [hybridization probes and said background probes are bound to] substrate is an array surface.

12. (Amended) The [method] assay of claim 10, [wherein the] wherein said target [nucleotide sequence is] nucleic acids are directly labeled [with said detectable label].

13. (Amended) The [method] assay of claim 10, [wherein the] wherein said target [nucleotide sequence is] nucleic acids are indirectly labeled [with said detectable label].

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14. (Amended) The [method] assay of claim 10, wherein said [signal is] signals are detected by colorimetric, fluorimetric, chemiluminescent or bioluminescent techniques.

15. (Amended) The [method] assay of claim 10, wherein the background [probes] features comprise probes selected from the group consisting of empirically observed inactive probes, probes forming stable intramolecular structures, short probes, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units.

16. (Amended) The [method] assay of claim 15, wherein the background [probes] features comprise [empirically observed inactive] probes selected from the group consisting of:

CAGAGGAAGAGAATCTCCGCAAGAA (SEQ ID NO: 5);
GAATCTCCGCAAGAAAGGGGAGCCT (SEQ ID NO: 6);
CGAGCTGCCCCCAGGGAGCACTAAG (SEQ ID NO: 7);
CCAGGGAGCACTAAGCGAGCACTGC (SEQ ID NO: 8);
TGAATGAGGCCTTGGAACTCAAGGA (SEQ ID NO: 9);
AAGGATGCCCAGGCTGGGAAGGAGC (SEQ ID NO: 10);
AGGCTGGGAAGGAGCCAGGGGGGAG (SEQ ID NO: 11);
GGAGCCAGGGGGGAGCAGGGCTCAC (SEQ ID NO: 12);
TGGGCTACACTGAGCACCAGGTGGT (SEQ ID NO: 13);
AATATGATGACATCAAGAAGGTGGT (SEQ ID NO: 14);
ATCCCTGAGCTAGACGGGAAGCTCA (SEQ ID NO: 15);
AACTGTGGCGTGATGGCCGCGGGGC (SEQ ID NO: 16);
GTGTGAACCATGAGAAGTATGACAA (SEQ ID NO: 17); and
TTCGTCATGGGTGTGAACCATGAGA (SEQ ID) NO: 18).

17. (Amended) The [method] assay of claim 15, wherein the background [probes] features comprise probes [forming stable intramolecular structures, wherein the probes are] selected from the group consisting of:

GCTAGCGAAAGCTAGC (SEQ ID NO: 24);

GCGAGCGAAAGCGAGC (SEQ ID NO: 25);

GCAGGCGAAAGCAGGC (SEQ ID NO: 26);

GCAGGGGAAAGCAGGC (SEQ ID) NO: 27); and

GCATACCGAAGCACGC (SEQ ID NO: 28).

18. (Amended) The [set] assay of claim 15, wherein the background [probes] features comprise [short probes, wherein the] probes [are] selected from the group consisting of:

AACCATGAGAAGTATGACAA (SEQ ID NO: 29);

TGAGAAGTATGACAA (SEQ ID NO: 30);

AGTATGACAA (SEQ ID NO: 31); and

GACAA (SEQ ID NO: 32).

19. (Amended) The [method] assay of claim 15, wherein the background [probes] features comprise reverse polarity nucleotide analog[s] probes.

20. (Amended) The [method] assay of claim 15, wherein the background [probes] features comprise abasic phosphodiester[s] probes or modified nucleotidic unit[s] probes.

21. (Amended) A method for estimating background noise in a nucleic acid hybridization assay, said method comprising:

(a) providing a sample of labeled target nucleic acids;

(b) contacting said sample under stringent hybridization conditions with a [set] collection of substrate bound nucleic acid features comprising [oligophosphodiester probes, wherein said features comprise hybridization features comprising]:

(i) hybridization probes [that selectively hybridize to a target nucleotide sequence], and

ii) background features [comprising background probes that do not selectively hybridize to said target nucleotide sequence and subtracting the];

(c) removing unhybridized target nucleic acids from said substrate;

(d) determining a background signal[, wherein said background] by detecting a signal [is an amount of signal generated from said] for each background feature[s, from the observed signal, wherein the observed signal is an amount of signal generated from contacting the target nucleotide sequence with said features comprising oligophosphodiester] and averaging said background feature signals.

22. (Amended) The method of claim 21 wherein said [hybridization probes and said background probes are bound to] substrate is an array surface.

23. (Amended) The method of claim 21, wherein said [signal is] signals are detected by colorimetric, fluorimetric, chemiluminescent or bioluminescent techniques.

24. (Amended) The method of claim 21, wherein the background [probes] features comprise probes selected from the group consisting of empirically observed inactive probes, probes forming stable intramolecular structures, short probes, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units.

25. (Amended) The method of claim 24, wherein the background [probes] features comprise [empirically observed inactive] probes selected from the group consisting of:

CAGAGGAAGAGAATCTCCGCAAGAA (SEQ ID NO: 5);
GAATCTCCGCAAGAAAGGGGAGCCT (SEQ ID NO: 6);
CGAGCTGCCCCCAGGGAGCACTAAG (SEQ ID NO: 7);
CCAGGGAGCACTAAGCGAGCACTGC (SEQ ID NO: 8);
TGAATGAGGCCTTGGAACTCAAGGA (SEQ ID NO: 9);
AAGGATGCCCAGGCTGGGAAGGAGC (SEQ ID NO: 10);
AGGCTGGGAAGGAGCCAGGGGGGAG (SEQ ID NO: 11);
GGAGCCAGGGGGGAGCAGGGCTCAC (SEQ ID NO: 12);

TGGGCTACACTGAGCACCAGGTGGT (SEQ ID NO: 13);
AATATGATGACATCAAGAAGGTGGT (SEQ ID NO: 14);
ATCCCTGAGCTAGACGGGAAGCTCA (SEQ ID NO: 15);
AACTGTGGCGTGATGGCCGCGGGGC (SEQ ID NO: 16);
GTGTGAACCATGAGAAGTATGACAA (SEQ ID NO: 17); and
TTCGTCATGGGTGTGAACCATGAGA (SEQ ID NO: 18).

26. (Amended) The method of claim 24, wherein the background [probes] features comprise probes [forming stable intramolecular structures, wherein the probes are] selected from the group consisting of:

GCTAGCGAAAGCTAGC (SEQ ID NO: 24);
GCGAGCGAAAGCGAGC (SEQ ID NO: 25);
GCAGGCGAAAGCAGGC (SEQ ID NO: 26);
GCAGGGGAAAGCAGGC (SEQ ID NO: 27); and
GCATACCGAAGCACGC (SEQ ID NO: 28).

27. (Amended) The [set] method of claim 24, wherein the background [probes] features comprise [short probes, wherein the] probes [are] selected from the group consisting of:

AACCATGAGAAGTATGACAA (SEQ ID NO: 29);
TGAGAAGTATGACAA (SEQ ID NO: 30);
AGTATGACAA (SEQ ID NO: 31); and
GACAA (SEQ ID NO: 32).

28. (Amended) The method of claim 24, wherein the background [probes] features comprise reverse polarity nucleotide analog[s] probes.

29. (Amended) The method of claim 24, wherein the background [probes] features comprise abasic phosphodiester[s] probes or modified nucleotidic unit[s] probes.

30. (Amended) A method of validating a test-background feature [comprising test-background probes], said method comprising:

(a) providing [an analyte suspected of containing the] a sample of labeled target [nucleotide sequence] nucleic acids;

(b) contacting [an aliquot of] said [analyte] labeled sample under stringent hybridization conditions [suspected of containing said target nucleotide sequence] with a [set] collection of substrate bound features comprising [oligophosphodiester probes, wherein said target nucleotide sequence is labeled with a detectable label capable of generating a measurable signal, and further wherein said features comprise]:

[(i) hybridization features comprising hybridization probes that selectively hybridize to a target nucleotide sequence,]

(i[i]) test-background features [comprising test-background probes] that [do] may or may not selectively hybridize to said target [nucleotide sequence] nucleic acids, and

(ii[I]) standard-background features [comprising standard-background probes] that [do] are known to not selectively hybridize to said target nucleic acids [nucleotide sequence];

(c) removing unhybridized target nucleic acids from said substrate;

[(c) detecting an observed signal, wherein the observed signal is an amount of signal generated from contacting the target nucleotide sequence with said features comprising oligophosphodiester probes;]

(d) [detecting] determining a test-background signal[, wherein said test-background] by detecting a signal [is an amount of signal generated from said] for each test-background feature[s] and averaging said test-background feature signals;

(e) [detecting] determining a standard-background signal[, wherein said standard-background] by detecting a signal [is an amount of signal generated from said] for each standard-background feature[s] and averaging said standard-background feature signals;

(f) comparing the amount of the test-background signal with the amount of the standard-background signal.

31. (Amended) The method of claim 30, [wherein the] wherein said target [nucleotide sequence] nucleic acids [is] are directly labeled [with said detectable label].

32. (Amended) The method of claim 30, [wherein the] wherein said target [nucleotide sequence] nucleic acids [is] are indirectly labeled [with said detectable label].

Cancel claim 33.

Add new claims 34-39.

--34. (New) A kit for use in the method of claim 10, said kit comprising:

an array having a plurality of background features, wherein said background features comprise probes selected from the group consisting of empirically observed inactive probes, probes forming stable intramolecular structures, short probes, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units.

35. (New) The kit according to claim 34, wherein the background features comprise probes selected from the group consisting of:

CAGAGGAAGAGAATCTCCGCAAGAA (SEQ ID NO: 5);
GAATCTCCGCAAGAAAGGGGAGCCT (SEQ ID NO: 6);
CGAGCTGCCCCCAGGGAGCACTAAG (SEQ ID NO: 7);
CCAGGGAGCACTAAGCGAGCACTGC (SEQ ID NO: 8);
TGAATGAGGCCTTGGAACTCAAGGA (SEQ ID NO: 9);
AAGGATGCCCAGGCTGGGAAGGAGC (SEQ ID NO: 10);
AGGCTGGGAAGGAGCCAGGGGGGAG (SEQ ID NO: 11);
GGAGCCAGGGGGGAGCAGGGCTCAC (SEQ ID NO: 12);
TGGGCTACACTGAGCACCAGGTGGT (SEQ ID NO: 13);
AATATGATGACATCAAGAAGGTGGT (SEQ ID NO: 14);
ATCCCTGAGCTAGACGGGAAGCTCA (SEQ ID NO: 15);
AACTGTGGCGTGATGGCCGCGGGGC (SEQ ID NO: 16);
GTGTGAACCATGAGAAGTATGACAA (SEQ ID NO: 17); and
TTCGTCATGGGTGTGAACCATGAGA (SEQ ID) NO: 18).

36. (New) The kit according to claim 34, wherein the background features comprise probes selected from the group consisting of:

GCTAGCGAAAGCTAGC (SEQ ID NO: 24);
GCGAGCGAAAGCGAGC (SEQ ID NO: 25);
GCAGGCGAAAGCAGGC (SEQ ID NO: 26);
GCAGGGGAAAGCAGGC (SEQ ID) NO: 27); and
GCATACCGAAGCACGC (SEQ ID NO: 28).

37. (New) The kit according to claim 34, wherein the background features comprise probes selected from the group consisting of:

AACCATGAGAAGTATGACAA (SEQ ID NO: 29);
TGAGAAGTATGACAA (SEQ ID NO: 30);
AGTATGACAA (SEQ ID NO: 31); and
GACAA (SEQ ID NO: 32).

38. (New) The kit according to claim 34, wherein the background features comprise reverse polarity nucleotide analog probes.

39. (New) The kit according to claim 34, wherein the background features comprise abasic phosphodiester probes or modified nucleotidic unit probes.--

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow claims 10-32 and 34-39, the only claims pending in this application.

AMENDMENTS

The amendment to the specification was made solely to denote that TRITON is a trademark and to provide the generic terminology requested by the Examiner. As such, no new material was added by this amendment and entry of the amendment is respectfully requested.

Claims 10-32 and 34-39 are pending in this application.

Claims 10-33 were examined and were rejected.

Claims 5-9 were canceled without prejudice to the filing of an application directed to the invention encompassed by these claims.

Claim 33 was canceled.

Claims 10-32 have been amended to more particularly point out and distinctly claim the invention, remove obvious typographical errors, and clarify claim language. Support for the amendments to claims 10, 21, and 30 can be found in the original claim and throughout the specification, particularly at: page 9, lines 18-24 (hybridization conditions); page 14, lines 12-20 (analyte is a sample which may contain single- or double-stranded nucleic acid molecules including a target nucleic acid); page 16, lines 2-3 (probes bound to a substrate); page 16, lines 21-28 (definition of "standard-background feature" and "test-background feature"); page 26, line 28 through page 27, line 9 (labeling step); page 27 line 12 through page 28, line 16 (hybridization conditions); page 30, lines 23-29 (hybridization conditions); page 31, lines 10-13 (removing step); page 38, lines 2-25 (compare average signal of test-background probe features to average signal from already validated background probe features (standard-background probe)); page 50, lines 22-24 (method uses average of signals from each background feature as the estimate of background signal for all features). Support for the amendment to claims 11 and 22 can be found throughout the specification, and in particular at: page 17, lines 57-27 ("'substrate'...denotes any solid support suitable for immobilizing one or more nucleic acid molecules..."). Support for the amendment to claims 12-13 and 31-32 can be found throughout the specification, and in particular at: page 14, lines 12-20 (analyte is a sample which may contain single- or double-stranded nucleic acid molecules including a target nucleic acid). Claims 14-20 were amended to make the claim language compatible with newly amended claim 10 on which they depend. Claims 23-29 were amended to make the claim language compatible with newly amended claim 21 on which they depend.

New claims 34-39 have been added. Support for new claim 34 can be found in original claims 15, 24, and 33 and throughout the specification, particularly at page 22, lines 1-5 (list of all background probe types found in the claim) and page 29, lines 7-17 (provision for a kit). Support for new claim 35 can be found in original claims 16 and 25 and throughout the specification, particularly at page 33, table 1 (list of all SEQ ID NOs listed in the claim). Support for new claim 36 can be found in original claims 17 and 26 and throughout the specification, particularly at page 37, table 3 (list of all SEQ ID NOs listed in the claim). Support for new claim 37 can be found in original claims 18 and 27 and throughout the specification, particularly at page 40,

table 5 (list of all SEQ ID NOs listed in the claim). Support for new claim 38 can be found in original claims 19 and 28 and throughout the specification, particularly at page 22, lines 3-4 (probes comprising reverse polarity nucleotide analogs); page 22, line 26 through page 23, line 1 (examples of reverse polarity nucleotide analogs); and page 41, lines 16-20 (examples of modified DNA probes include reverse polarity nucleotide analogs). Support for new claim 39 can be found in original claims 20 and 29 and throughout the specification, particularly at page 22, lines 4-5 (probes comprising abasic phosphodiesters or modified nucleotidic units); page 23, lines 3-17 (examples of abasic phosphodiesters or modified nucleotidic units); and page 41, lines 2-20 (examples of probes comprising abasic phosphodiesters or modified nucleotidic units).

Accordingly, no new material is added by the above amendments and new claims. As such, their entry by the Examiner is respectfully requested.

For the Examiner's convenience, a copy of the pending claims as amended is provided in an Appendix attached hereto.

REJECTIONS

35 U.S.C. §112, first paragraph

Claims 10-32 have been rejected under 35 U.S.C. §112, first paragraph, for the asserted reason that they contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which the invention pertains, or with which it is most nearly connected, to make and/or use the invention. These rejections are traversed as applied and as they may apply to the presently pending claims. The Applicant will individually address each specific rejection.

First, the Examiner asserts that claim 10 requires one of skill in the art to definitively label a target nucleic acid sequence when the skilled artisan is not even sure that such a sequence exists. In addition, the Examiner objects that there is no method step for achieving said labeling.

The Applicant has amended claim 10 to clarify the labeling of the target nucleic acid. Further, the amendment specifies that the entire sample of target nucleic acids is labeled. Thus, the amendments to claim 10 address the Examiner's concerns and this rejection of claim 10 under 35 U.S.C. §112, first paragraph, can be withdrawn.

Second, the Examiner asserts that claim 10 does not recite any means by which the skilled artisan is to be able to discriminate between, and independently measure, the signal from the target sequence and the background signal. In addition, claims 11-20, which depend on claim 10, do not enable one skilled in the art to make such measurements.

The Applicant has amended claim 10 to clarify that the nucleic acid features are bound to a substrate. Read in light of the specification, the skilled artisan would see that such binding is done with knowledge as to the location of each feature. Thus, one skilled in the art would know the location of both the hybridized labeled target sequence and the background features. The skilled artisan could then independently and discriminately measure both the observed signal and the background signal using the methods set forth in the instant invention. As such, the Applicant has enabled the claimed invention and respectfully requests that this rejection of claim 10 under 35 U.S.C. §112, first paragraph, be withdrawn.

Third, the Examiner objects that the claimed method does not recite any conditions under which the hybridization reaction is to take place. Further, the Examiner asserts that neither the claims nor the specification set forth in sufficient detail an enabling disclosure whereby one of skill in the art would be able to perform the claimed assay without having to take such issues into consideration.

The law is clear that "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." United States v. Telectronics, Inc., 8 USPQ 2d 1217, 1233 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989). See also, Genentech, Inc. v. Novo Nordisk, 42 USPQ 2d 1001 (Fed. Cir. 1997), cert. denied, 522 U.S. 963 (1997); Scripps Clinic and Research Foundation v. Genentech, Inc., 18 USPQ 2d 1001 (Fed. Cir. 1991). The Applicant respectfully submits that the specification and the amended claims, coupled with the information known in the art, would enable one of skill in the art to use the invention without undue experimentation.

The claims have been amended to specify that hybridization takes place under stringent conditions. The specification discusses hybridization conditions in several places. In particular, page 9, lines 18-24 state:

> Increased stringency is achieved by elevating the temperature, increasing the ratio of co-solvents, lowering the salt concentration, and

> the like...Conditions for hybridization typically include high ionic strength solution, controlled temperature, and the presence of carrier DNA and detergents and divalent cation chelators, all of which are well-known in the art.

Page 27 line 12 through page 28, line 16 state:

> Hybridization generally takes from about 30 minutes to about 24 hours, and occurs at the highest specificity approximately 10-25°C below the temperature (T_m) at which the nucleotide hybrid is 50% melted. The T_m for a particular hybridization pair will vary with the length and nature of the nucleotides and may be readily determined by those of ordinary skill in the art...it is well-known in the art that numerous equivalent conditions can be employed to establish a particular stringency by varying, for example, the following factors: the length and nature of probe and target sequences, base composition of the various sequences, concentrations of salts and other hybridization solution components, the presence or absence of blocking agents in the hybridization solution..., hybridization reaction temperature and time parameters, as well as, varying wash conditions. The selection of a particular set of hybridization conditions is well within the skill of a person of ordinary skill in the art (see, for example, Sambrook, et al., *Molecular Cloning: A Laboratory Manual*, Second edition, (1989) Cold Spring Harbor, N.Y.).

In addition, page 30, lines 23-29 recite the specific hybridization conditions used for Example 1. Thus, the Applicant has set forth numerous factors to be considered by one skilled in the art in choosing hybridization conditions. Further, the Applicant has specified the exact hybridization conditions used to perform Experiment 1.

Thus, one reasonably skilled in the art could make or use the present invention from the disclosures in the patent coupled with information known in the art without undue experimentation. As such, the Examiner is respectfully requested this rejection under 35 U.S.C. §112, first paragraph.

Fourth, the Examiner contends that claims 21-29 are not adequately enabled by the disclosure because they do not recite adequate method steps to allow one of skill in the art to estimate background noise.

The Applicant has amended claim 21 to clarify the steps required to arrive at an estimate of the background noise. Thus, one skilled in the art would be able to use the methods of the claimed invention to estimate background noise. As such, the Applicant has enabled the claimed invention and respectfully requests that this rejection of claims 21-29 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claim 33 has been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that claim 33 "has sufficient breadth of scope so [as] to encompass any probe that would detect any target nucleic acid, be it known or unknown to one of skill in the art at the time the subject application was filed." Further, the Examiner has interpreted "background features" as encompassing non-target nucleic acid probes which could bind to a variety of non-target nucleic acids during a hybridization assay. This rejection is traversed as applied and as it may apply to the presently pending claims.

The Applicant has clearly defined what constitutes a background feature on page, 16 lines 15-20, and further defined what constitutes a background probe on page 21, line 25 through page 22, line 5. In addition, the various types of background probes themselves are defined on, for example, page 22, line 6 through page 23, line 17. The Applicant has also reduced the present invention to practice by, for example, performing assays, detecting background signal and observed signal, and then removing this background signal from the observed signal. Further, the Applicant has identified specific nucleotide sequences that fulfill the requirements of background probes. Examples of these sequences are SEQ ID NOs: 5-18, 24-28, and 29-32. As such, a set of claims directed toward a kit for use in the method of claim 10 is not beyond the scope of the specification. Therefore, the Applicant respectfully requests the withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

35 U.S.C. §112, second paragraph

Claims 10-20 and 30-32 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. This rejection is traversed as applied and as it may apply to the presently pending claims. The Applicant will individually address each specific rejection.

First, the Examiner contends that claim 10 is indefinite with respect to which "feature" is intended by the reference to "said features." In addition, claims 11-20, which depend from claim 10 are similarly indefinite.

In order to expedite prosecution, the Applicant has amended claim 10 to remove the reference to "said feature" that the Examiner found to be objectionable. Thus, claim 10 is not indefinite and the Applicant respectfully requests that this rejection of claim 10 under 35 U.S.C. §112, second paragraph, be withdrawn.

Second, the Examiner contends that claim 30 is indefinite with respect to just what constitutes "test-background probes" and "standard-background probes." In addition, claims 31 and 32, which depend from claim 30 fail to overcome this issue and are similarly indefinite.

The Applicant has amended claim 30 to clarify what is meant by the claim. In addition, the Applicant refers the Examiner to page 16, line 21 through page 17, line 2, which contain the definition of "standard-background features" and "test-background features." Thus, when claim 30 is read in light of the specification, it is not indefinite. As such, this rejection of claims 30-32 under 35 U.S.C. §112, second paragraph, can be withdrawn.

Claims 10-32 have been rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps, with such omissions amounting to a gap between the steps. This rejection is traversed as applied and as it may be applied to the presently pending claims. The Applicant will individually address each specific rejection.

First, claims 10-20 have been rejected for omitting how to label that which is only suspected of being present, how to differentially detect target and non-target signal, how to remove unbound label from the assay mixture, and how the various background probes are made and used.

The Applicant has addressed all of these issues by clarifying the claim language such that the entire sample of target nucleic acids is labeled, the hybridization probes and background features are bound to a substrate allowing the skilled artisan to independently and discriminately measure the signal from each, and there is clearly a removing step. In addition, the Applicant believes that the amendment to claims 16-18 have addressed the Examiner's final reason for rejecting claims 10-20. As such, the Applicant respectfully requests that this rejection of claims 10-20 under 35 U.S.C. §112, second paragraph, be withdrawn.

Second, claims 21-29 have been rejected for omitting how the nucleic acid assay is to be performed, how to differentially detect target and non-target signal, and how the various background probes are made and used.

The Applicant has addressed all of these issues by clarifying the claim language such that the assays are carried out under stringent hybridization conditions and the hybridization probes and background features are bound to a substrate allowing the skilled artisan to independently and discriminately measure the signal from each. In addition, the Applicant believes that the amendment to claims 25-28 have addressed the Examiner's final reason for rejecting claims 21-29. Therefore, the Applicant respectfully requests that this rejection of claims 21-29 under 35 U.S.C. §112, second paragraph, be withdrawn.

Third, claims 30-32 have been rejected for omitting how the nucleic acid assay is to be performed, how to differentially detect target and non-target signal, and what the composition of the various features is and under what conditions they are to be used.

The Applicant has addressed all of these issues by clarifying the claim language such that the assays are carried out under stringent hybridization conditions, the hybridization probes and background features are bound to a substrate allowing the skilled artisan to independently and discriminately measure the signal from each, and the composition of the various features is readily apparent. Therefore, the Applicant respectfully requests that this rejection of claims 30-32 under 35 U.S.C. §112, second paragraph, be withdrawn.

CONCLUSION

The presently pending claims have been amended to place them in better condition for allowance. No new matter has been added by the amendments to claims 10-22 and 24-32, nor by the addition of new Claims 34-39. In addition, the claims are enabled by the specification, do not contain subject matter that was not in possession of the inventors at the time the application was filed, and are not indefinite. Accordingly, the Applicant respectfully requests withdrawal of the rejections and allowance of the pending claims.

If the Examiner finds that a Telephone Conference would expedite prosecution of this application, he is invited to contact the Mr. Gordon Stewart at (650) 236 2386.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 and 1.17 that may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,

Date: 8.25.00

By: _____
Bret E. Field
Registration No. 37,620

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